Case Reports

Antibiotic-Induced Acute Renal Failure Associated With an Elevated Serum Lactic Dehydrogenase Level of Renal Origin

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MANY BODY TISSUES contain the enzyme lactic dehydrogenase (LDH) but only in three (myocardium, erythrocytes and kidney) is there a predominance of the isoenzyme LDH_1.[1] An elevated level of LDH, with the isoenzyme fraction LDH_1 greater than that of LDH_2, has been a well-recognized consequence of embolic renal infarction.[1,2] In the following report, a patient with antibiotic-induced nephrotoxicity showed an increased serum LDH level of renal origin.

Report of a Case

The patient, a 54-year-old man, was admitted to the orthopedic service with a shotgun wound to the left thigh and fracture of the left femur. A regimen of cefazolin, 1 gram given intravenously every eight hours, and gentamicin sulfate, 100 mg given intravenously every eight hours, was started for the wound infection. The patient had baseline blood urea nitrogen (BUN) and creatinine levels of 14 and 1.2 mg per dl, respectively. After two days of therapy, he had had a peak gentamicin concentration of 5.4 μg per dl and a trough gentamicin concentration of less than 1 μg per dl. No further gentamicin measurements were obtained. After ten days of antibiotic therapy, the serum creatinine level rose to 2.6 mg per dl; the regimen of cefazolin and gentamicin was discontinued four days later. At this time the serum creatinine level was 8.5 mg per dl, the LDH value was 775 units per liter (normal 25 to 200) and the serum creatine kinase (CK) level was 558 units per liter (normal 0 to 175). Isoenzyme fractionation showed that the CK was entirely from skeletal muscle (MM). Urine analyses done by the renal consultant on two separate occasions showed only trace protein. Three days later, when the total serum LDH level was 594 units per liter, the LDH_1 was 46, LDH_2 37, LDH_3 13, LDH_4 2 and LDH_5 2 units per liter. The patient's electrocardiogram (ECG) showed a normal sinus rhythm, unchanged from an ECG on admission. The hematocrit was unchanged; serum haptoglobin and indirect bilirubin levels were normal. There were no eosinophils in blood or urine specimens. A renal isotope scan done to investigate embolic infarction showed homogeneous renal images with diminished blood flow to both kidneys. During the period of acute renal failure, the patient's urine volume was 1,000 to 2,000 ml per day. After four hemodialysis treatments over ten days, the patient's BUN and creatinine values began to decline and the dialysis was stopped. The patient's serum creatinine and total serum LDH levels 45 days after starting antibiotics and 31 days after stopping the therapy were 1.4 mg per dl and 150 units per liter, respectively.

ABBREVIATIONS USED IN TEXT
BUN = blood urea nitrogen
CK = creatine kinase
ECG = electrocardiogram
LDH = lactic dehydrogenase

Discussion

This patient had a sustained elevation in serum LDH during an episode of acute renal insufficiency. LDH is an almost ubiquitous enzyme, found in brain, liver, muscle, kidney, leukocytes and erythrocytes. In the present case, there was no clinical suspicion of a cerebrovascular accident, and liver injury was not present. The patient's wound may have been the source of the elevation in CK, but muscle injury could not be responsible for the elevated LDH level because the ratio of LDH to CK (about 1:10 in cases of muscle injury)[3] was inconsistent with criteria for rhabdomyolysis. As the patient had no symptoms of a myocardial infarction, the ECG was normal and unchanged from admission and the myocardial isoenzyme fraction of CK (CK-MB) was absent, the diagnosis of myocardial infarction was untenable. Because the hematocrit was stable and haptoglobin and bilirubin levels were normal, hemolysis was also eliminated from the differential diagnosis. The elevation in serum LDH was most consistent with the obvious and clinically severe renal injury that developed during prolonged administration of antibiotics. Fractionation of serum LDH provided more definitive evidence of its origin. The finding of an LDH level that was elevated and an LDH_1 that was higher than the LDH_2 value were consistent with hematologic, myocardial or renal injury. Only the kidney was justifiable as a source in the aforementioned clinical and laboratory context.

Renal injury was attributable in this case to tubular toxicity from gentamicin therapy, which was possibly accentuated by concurrent cephalosporin administration.[4] Gentamicin accumulates in cells of the proximal tubules and can cause damage that is detectable by electron microscopy.[5] As a consequence of tubular damage, urinary total LDH and LDH_1 levels can be increased during intramuscular aminogly-

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coside therapy.[6] This observation gives further support to a putative relationship between severe aminoglycoside toxicity and an elevation in the serum LDH_1 levels. Although renal failure was attributed to aminoglycoside therapy, a renal biopsy was not done to provide conclusive proof for this diagnosis. In the absence of fever, rash, eosinophilia or eosinophiluria, a drug-induced interstitial nephritis from cefazolin would be unlikely but not impossible.[7] Either antibiotic could have led to damaged renal tubular epithelium and have caused the release of renal LDH.

Elevations in serum LDH levels of renal origin have been attributed exclusively to embolic renal infarction,[1,2] usually in patients with cardiomegaly and atrial fibrillation or myocardial infarction.[7] Embolic occlusion of a renal artery can lead to complete unilateral renal infarction and elevation of the serum LDH level to 2,000 to 2,500 units per liter.[7] In the present case, lack of a suitable clinical context and absence of a focal loss of renal parenchyma as shown by a renal isotope scan mitigated against embolic renal infarction and supported the diagnosis of antibiotic-induced acute renal insufficiency that caused release of renal LDH.

In this patient, azotemia required dialysis and lasted several weeks, but the relationship, if any, of the elevation in renal LDH to the course and prognosis of the acute renal insufficiency remains unknown. Antibiotic-induced acute renal failure should be included in the differential diagnosis of an elevation in the serum LDH level, and isoenzyme fractionation should be done to help confirm that the LDH is of renal origin.

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Young's Syndrome

An Association Between Male Sterility and Bronchiectasis

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IT HAS BEEN well established that there are associations between bronchiectasis or chronic bronchitis and male infertility.[1,2] The best known examples are cystic fibrosis[1] and the immotile cilia syndrome.[2] Young's syndrome was described in 1970, consisting of chronic lung disease, obstructive azoospermia, normal spermatogenesis and characteristic epididymal findings.[3] Unlike the immotile cilia syndrome, Young's syndrome is characterized by azoospermia and normal ultrastructure of cilia. It differs from cystic fibrosis by a normal sweat test and normal pancreatic function.[4] We report the case of a patient with the clinical features of Young's syndrome.

Report of a Case

A 64-year-old man, white and a nonsmoker, started having recurrent lung infections at age 20. Since then he has had a chronic cough productive of one to two cups of yellowish sputum daily. A bronchogram done 30 years ago showed bilateral bronchiectasis. He has always had postnasal drip and a mucopurulent nasal discharge. He had normal sexual development, libido and potency. Despite being sexually active and married twice (8 and 11 years' durations), he has had no children. The patient used condoms, however, during his first marriage because children were not wanted; the second marriage has been to a postmenopausal woman six years his senior. There is no history of asthma, occupational exposure to toxins or scrotal trauma or infection, nor is there a family history of asthma, bronchitis, bronchiectasis, chronic lung disease or infertility.

ABBREVIATIONS USED IN TEXT

AAT = α_1-antitrypsin
FEV_1 = forced expiratory volume in one second
FSH = follicle-stimulating hormone
FVC = forced vital capacity
Ig = immunoglobulin
TIC = trypsin inhibitory capacity

On physical examination, he was well developed, well nourished and had mild clubbing of the fingers. Auscultation of the lungs showed early inspiratory crackles in both lower lung fields and mild diffuse wheezing. The external genitalia were normal with normal-sized testes of normal consistency and a palpable right epididymis and vas deferens. The left epididymis, however, was hypoplastic with cystic distention in the head.

Laboratory studies showed a slightly increased serum immunoglobulin (Ig) A level (646 mg per dl) and normal IgG and IgM values. A sputum culture grew *Hemophilus parainfluenzae*. A sweat test done by pilocarpine iontophoresis showed a normal sweat chloride value of 34 mEq per liter. α_1-Antitrypsin (AAT) studies showed an MS phenotype and a serum trypsin inhibitory capacity (TIC) of 1.063 units per ml. The heterozygous S variant of AAT is not known to be associated with any disease state, and in this instance the associated serum TIC value is normal (>0.95 units per ml). The serum follicle-stimulating hormone (FSH) level was 11.0 mIU per ml (normal 1 to 15) and the testosterone level was 540 ng per dl (normal 400 to 1,000). Antisperm antibodies were absent from the serum. On semen analysis there was complete azoospermia.

Pulmonary function testing showed moderate obstructive

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